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Profiles of children with Down syndrome who meet screening criteria for Autism Spectrum Disorder (ASD): a comparison with children diagnosed with ASD attending specialist schools.

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Abstract

Background. Recent research suggests that around 16% to 18% of children with Down syndrome also meet diagnostic criteria for autism spectrum disorder (ASD). However, there are indications that profiles of autism symptoms in this group may vary from those typically described in children with ASD.

Method. Rates of autism symptoms and emotional and behavioural problems among children with DS who screened positive for ASD on the Social Communication Questionnaire (SCQ) (n = 183) were compared with a group of children with clinical diagnoses of ASD (n = 189) attending specialist schools in the UK. Groups were matched for age and approximate language level (use of phrase speech).

Results. Profiles of autistic symptoms in the two groups were generally similar, but children with DS meeting ASD cut-off on the SCQ tended to show fewer problems in reciprocal social interaction than those in the ASD group. They also showed slightly lower rates of emotional and peer related problems. The results mostly confirm findings from a previous study in which the original validation sample for the SCQ was used as a comparison group.

Conclusions: Findings suggest that children with DS who meet screening criteria for ASD show similar profiles of communication and repetitive behaviours to those typically described in autism. However, they tend to have relatively milder social difficulties. It is important that clinicians are aware of this difference if children with DS and ASD are to be correctly diagnosed and eligible for specialist intervention and education services.

Keywords: autism spectrum disorder, Down syndrome, behavioural disturbance, strengths and difficulties questionnaire, social communication questionnaire

Children with Down Syndrome (DS) are typically characterized as having relatively good social skills, whilst autism is associated with a range of social impairments. Thus, in the past, it was often assumed that the two conditions rarely co-occurred (c.f. Rutter, 1985). However, recent research indicates relatively high rates of autism spectrum disorder (ASD) in children with DS, with prevalence estimated at around 16% to 18% (Channell et al., 2015; DiGuiseppi et al., 2010; Lowenthal et al., 2007; Richards, et al., 2015). This is considerably higher than estimated rates of ASD in the general population (approximately 1% to 1.5%; Baird et al. 2006; Christensen et al., 2016].

Several studies have compared the cognitive and behavioural profiles of individuals with "typical" DS with those of individuals with DS who either have a comorbid diagnosis of ASD or who score positively on ASD screening measures. These indicate that individuals with the dual diagnosis are likely to show higher levels of behavioural disturbance (e.g. Capone et al., 2005; Ji et al., 2011; Warner et al., 2014); more repetitive and stereotyped behaviours (e.g. Moss et al., 2013b); poorer social, language and adaptive skills (e.g. Dressler et al., 2011; Magyar et al., 2012; Molloy et al., 2009; Warner et al., 2014) and greater frequency of regression (Castillo et al., 2008; Warner et al., 2014).

There are fewer studies comparing profiles of individuals with a diagnosis of autism with those of children with both DS and ASD. Some suggest that, compared with ASD only groups, individuals with the dual diagnosis have poorer expressive language and imitation skills, are more hyperactive, and have greater difficulties with change (Dressler et al., 2011). Age of regression, if it occurs, also tends to be significantly later (around 4-5 years in children with the dual diagnosis, under 2 years in children with "idiopathic" ASD; Castillo et al., 2008). In contrast, Moss et al. (2013b) found few group differences although the dual diagnosis group showed more interest in their surroundings. However, such comparisons are limited by small sample sizes and wide variability in participants' ages and in the measures used.

There has been only one large-scale comparison of children with ASD and children with DS who also meet screening criteria for ASD (Warner et al., 2014). They compared

profiles of autism characteristics in children with DS who screened positive for ASD (n=183; age 6 to 15 years) on the Social Communication Questionnaire (SCQ; Rutter, et al., 2003) with data on the reference sample of 160 individuals with autistic spectrum or other pervasive developmental disorders that was originally used to determine the diagnostic validity of the SCQ (Berument et al., 1999). Compared with the SCQ validation group, children with DS who scored above cut-off for ASD were significantly *less* impaired in their use of gesture, imitation and imitative social play and in several aspects of social reciprocity (eye gaze, smiling, shared enjoyment, offering comfort, social overtures, response to other children). They showed significantly *more* communication impairments, such as pronoun reversal, use of neologisms and social chat, and they had higher rates of compulsions and rituals. These differences, however, may have been partly due to the characteristics of the Berument et al (1999) reference group. Their age range was much wider (4 to 40 years) and participants were highly selected individuals involved in family genetic studies and thus possibly less representative of the general population of children with ASD.

In the present study our aims were to expand on the Warner et al. comparison by using a UK school-based sample of children with clinical diagnoses of ASD, matched for age and approximate verbal ability (i.e. whether or not they used phrase speech). We then aimed to compare the present findings with those from the validation sample analysis. A secondary aim was to compare data on reported rates of emotional and behavioural problems in the two groups.

Method

Participant recruitment

DS + ASD group

Parent members of the UK Down's Syndrome Association participated in a postal survey of social and behavioural characteristics of children with DS aged 6-15 years. Of 1,382 families contacted, 499 (36%) returned complete forms. From this sample, 183 children met the threshold for ASD on the SCQ (i.e. score of ≥ 15. See below for measures and Warner at al., 2014 for study details). This is subsequently referred to as the DS+ASD group. As this was

a postal survey, data on IQ were not available and ratings of language level were based on the SCQ (see below).

ASD comparison group

The comparison group was selected from a database of 759 children (age 4-19 years) attending 10 specialist autism schools in or around London, UK (the *Pan-London Autism School Network Research (PLASN-R) group).* PLASN-R is a network of researchers and educators that aims to improve autism expertise across educational research and practice (Parsons et al., 2013; Salomone et al., 2014). All pupils attending PLASN schools have a statement of special educational needs (SEN)[1] with autism as their primary diagnosis. Children were selected from the main database if they were within the same age range as the DS group and scored at or above the SCQ cut-off for ASD (see below; total n=189). Although no direct information on intellectual ability was available, school admission requirements meant that all would be considered to have some degree of intellectual impairment, ranging from severe to mild. Ratings on language level were obtained from the SCQ.

Ethical approval

Identifying data on all participants were removed for the present analysis. Ethical approval for the studies was granted by the Research Ethics Committees of King's College London (Psychiatry, Nursing & Midwifery Subcommittee) and the Institute of Education, University of London.

Measures

As all data were obtained via parental surveys and, as the aim was to recruit as large and representative group as possible, it was necessary to limit the number of different questionnaires distributed. Discussions within the PLASN network raised concerns that

[1] In the UK, local authorities record annual assessments on a "statement of SEN" which describes the child's diagnosis and needs and the arrangements that the school has to make in order to meet them.

including measures of IQ and/or details of diagnostic ascertainment would risk a decrease in response rates. Thus, no data were collected on cognitive ability, autism sub-types or comorbid/other genetic diagnoses. The following instruments were selected:

Autism symptoms: The Lifetime version of the Social Communication Questionnaire (SCQ; Rutter et al., 2003) was used to identify characteristics associated with ASD. The SCQ is a 40-item parent-report screening measure with items divided into 3 subdomains: Reciprocal Social Interaction, Communication, and Restricted, Repetitive and Stereotyped Patterns of Behaviour (RRSB). The suggested cut-offs are ≥ 22 for autism and ≥ 15 for ASD. Item level validity is good (Berument et al., 1999; Bölte et al., 2008); sensitivity and specificity in school-aged samples are relatively high (.86 and .78 respectively; Charman et al, 2007), and Magyar et al. (2012) reported specificity and sensitivity >.80, together with good convergent and discriminant validity, in a large sample (n>400) of children with DS.

The SCQ also provided an approximate estimate of verbal ability (can/cannot talk using short phrases/sentences).

Behavioural and emotional difficulties: The Strengths and Difficulties Questionnaire (Parent version, SDQ; Goodman, 1997) is a 25-item questionnaire that screens for the presence of hyperactivity, emotional symptoms, conduct problems and peer problems in children (4 -17 years). The SDQ has good psychometric properties for identifying children with behavioural and emotional difficulties in clinical and community populations (Goodman, 2001; Stone et al., 2010).

Statistical analysis

Odds ratios were calculated to determine SCQ item-specific differences between the DS+ASD and ASD comparison group (cf Hall et al.,2010; Moss et al., 2013a; Warner et al., 2014). The number of children in each group who scored on an individual SCQ item was used to calculate odds ratios (OR's). An OR significantly > 1.0 (i.e. outside the 99% confidence interval for that item) indicated that the symptom was significantly more likely to be present in the DS+ASD group; OR significantly <1.0 indicated that the symptom was significantly more likely to be present in the ASD group. A second odds ratio analysis,

excluding non-verbal children, was run for the 'social chat' item in the Communication domain as this item, unlike other SCQ communication items, was not subject to verbal ability screening.

Data were tested for normality using Kolmogorov-Smirnov tests and visual inspection of histograms. Homogeneity of variance between the comparison groups (i.e. DS+ASD and ASD) was tested using Levene's tests. If assumptions of normality/homogeneity of variance were met parametric tests were used; otherwise non-parametric analyses were conducted.

Significance level was set at $p<.05$. Effect sizes (Cliff's d or Cohen's d) were interpreted as small = .10, medium = .30, and large ≥ .50 (Field, 2005).

Results

1.Group matching

Group mean ages were similar (DS+ASD 10.9 years, sd 2.8; ASD 10.7 years, sd 2.9; t=.44; p=.05); the proportions using phrase speech were also comparable (65% vs. 69%; X^2 =0.77; p=.37). However, there were somewhat fewer males in the ASD+DS group (67% vs. 82%, X^2 =3.86; p=.03).

2.SCQ scores and profiles of autism symptoms.

Table 1 about here

Compared with the ASD sample, the DS+ASD group had a somewhat lower mean SCQ total score and mean scores on each of the other domains were also lower, with moderate to large effect sizes (See Table 1)

Table 2 about here

Table 2 summarises the OR analysis of SCQ items (see Supplementary figures for visual representation of the analysis). There were few group differences in communication problems but the DS+ASD group was significantly less likely to show difficulties in imitation and imitative social play. In the Social domain the DS+ASD group was significantly less likely to show impairments in eye-gaze, facial expression, social smiling and general quality of social overtures; they were more likely to offer comfort to others and to respond to

approaches by other children. In the RRSB domain the only significant difference was for compulsions and rituals, which were more likely in the DS+ASD group.

3.Comparisons with findings from the Berument et al. (1999) validation sample.

A previous study (Warner et al., 2014) compared profiles of children in the DS+ASD group with the Berument et al. (1999) reference sample. They found similar levels of autism severity (mean SCQ: DS+ASD group=21.3; Reference group=22.3) but, compared with the validation sample, the DS+ASD group was significantly less likely to show problems related to imitation and imitative social play (OR's = 0.3) and these differences were replicated in the present comparison. In contrast, in the earlier Warner study, the DS+ASD group had been reported to show *more* communication problems related to the use of neologisms (OR 2.2), pronoun reversal (OR 4.5) or social chat (OR16.9); these differences did not emerge in the present analysis involving groups of similar age. In the Social domain, of the group differences reported by Warner et al. (i.e. DS+ASD group l*ess* impaired in eye-gaze, social smiling, shared enjoyment, offering comfort and social overtures (all OR's 0.05) and response to other children (OR 0.4), only the item "seeking to share enjoyment" no longer showed any group difference. In the RRSB domain the increased risk of compulsions and rituals in the DS+ASD group (OR 2.9) was again replicated.

4. *Behavioural and emotional difficulties*

Table 3 about here

A secondary aim of the study was to compare rates of behavioural and emotional difficulties as measured by the SDQ. The ASD group was rated as showing rather more behaviour problems overall; they also had more emotional and peer problems than the DS+ASD group. However, although the differences were significant, effect sizes were small (See Table 3).

Discussion

There is evidence from several studies that individuals with a comorbid diagnosis of DS and ASD show more cognitive, social and behavioural difficulties than individuals with "typical"

DS (Channell et al., 2015). However, studies comparing the dual diagnosis group with individuals with a diagnosis of autism alone have produced inconsistent findings. The present study compared two relatively large groups of children with/without DS scoring at or above the SCQ cut-off. Although total scores on the SCQ, and scores in each of the three domains (Social, Communication, Repetitive behaviours), were lower in the DS+ASD group rather different profiles of impairments emerged. Thus, of the 14 items in the Communication domain, only imitation and use of gesture were *less* impaired in the DS+ASD group; otherwise group profiles were similar. In contrast, among the 15 SCQ Social items, almost half (n=7) were significantly *less* likely to occur in the DS+ ASD group. In the RRSB domain, comprising 8 items, only one (Compulsions and Rituals) was *more* evident in the DS+ASD group. SDQ scores also indicated that the DS+ASD group was less likely to show emotional and peer-related problems, although effect sizes were small.

With some exceptions (see Results above) these findings are similar to those of Warner et al. (2014) using the original validation sample as their comparator. Thus, the present study strengthens conclusions about the characteristics of children with Down syndrome who meet criteria for ASD. Overall it appears that differences tend to be most marked in the reciprocal social interaction domain, with the DS+ASD group being generally more overtly sociable than children with so called ”idiopathic” autism[2]. Profiles of communication and ritualistic behaviours are generally similar in both groups.

The findings also suggest that data from the original SCQ validation sample remain a useful comparator for exploring patterns of autism symptomatology in “atypical” autism groups. This is despite the heterogeneity of that sample, and the fact that diagnostic classification has changed somewhat since the validity data were collected. Nevertheless, closer matching of groups with regard to age and, if possible, intellectual ability, is likely to increase the reliability of findings.

[2] Note: we chose not to use the term “idiopathic” in the present study because of the growing number of genetic/chromosomal abnormalities that are now related to the disorder. Thus we do not know if autism was, or was not, the primary condition in the sample participants.

Finally, data from the SDQ on behavioural and emotional problems at least partially confirm previous reports of higher rates of behavioural problems in children with the dual diagnosis. However, it should be noted that there were no differences found in conduct and hyperactivity problems and effect sizes for differences in relation to emotional and peer problems were small.

As in any postal survey, the study has a number of methodological problems that limit the strength of the conclusions:

1) Reliance on survey data introduces increased likelihood of bias, since response rates tend to be low, and members of parent support groups may not be representative of parents in the wider population.
2) All data were based on parent reports, with no independent validation of behavioural or other difficulties.
3) In the ASD group there was no independent diagnostic ascertainment and no systematic information on additional genetic or other possible aetiological conditions. (e.g. Fragile X; Hall et al., 2010) that might have affected the group profiles. One child in the school sample had Down syndrome but it was not possible to delete his/her data without infringing anonymity.
4) No IQ data were collected in either group. However, enrolment in specialist autism schools in the UK requires that all children are clinically ascertained as meeting formal diagnostic criteria for autism and have additional intellectual impairments. Studies of children with DS also indicate that the majority have mild to moderate intellectual disability (IQ scores typically 40-70; Hodapp, 1999)
5) Although the groups were well matched on age, verbal matching was based only on a single dichotomous variable (not/using phrases speech).
6) Finally, there was a small but significant group difference of 4 points on the total SCQ score (ASD>DS+ASD) and, as reported in other studies, there were proportionately more males in the DS+ASD group. How these differences may have affected the findings is uncertain.

Clinical implications

Despite the above caveats, this study is the largest to date to compare profiles of autism symptoms between children with clinical diagnoses of ASD and children with DS who meet cut-off for ASD on a well standardised screening instrument (the SCQ). The findings indicate the importance of focusing, not only on total scores for ASD symptoms, but on the patterns of symptomatology shown by different groups of children. Overall, although scores on the SCQ tended to be higher in the non-DS children, the two groups showed a similar range of difficulties related to communication problems and repetitive and stereotyped behaviours. In contrast, the social interaction skills of the DS+ASD children tended to be less impaired, which is likely related to the higher sociability of children with DS more generally (Dykens et al., 2006). This pattern of superficially better social skills, together with the belief among some that ASD and DS rarely co-occur (Rasmussen et al., 2001), adds to the risk that children with Down syndrome who have ASD may not be correctly diagnosed. In turn this can result in inadequate intervention and educational provision and lack of appropriate support for families. It was notable, in the present study, that only one child in the ASD school sample had Down syndrome, suggesting that, in the UK, few children with the dual diagnosis receive autism-specific education. Today, children with a clinical diagnosis of ASD have a far better chance of specialist schooling and access to early intervention programmes than in the past. The same opportunities must also be available to children with DS who have ASD but this requires wider recognition and acknowledgement of the increased risk of ASD in this group.

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Table 1. SCQ scores in DS+ASD and ASD groups

SCQ	**Group**	**Mean(SD)**	**Group difference***
Total	DS+ASD	21.3 (5.4)	t=7.40; p<.001
	ASD	25.6 (5.6)	d=.77
Subscale			
Communication	DS+ASD	6.8 (2.0)	t=4.43; p<.001
	ASD	7.9 (2.4)	d=.46
Social	DS+ASD	8.2 (3.3)	t=6.71; p<.001
	ASD	10.3 (2.9)	d=.69
Repetitive behavior	DS+ASD	4.9 (1.8)	t=3.42; p<.01
	ASD	5.6 (1.9)	d=.35

*Independent t test, Cohen's d.

Table 2. SCQ odds ratio analysis (DS+ASD vs. ASD comparison group)

	SCQ Item[a]	OR[a]	99% CI
Communication	Conversation	1.33	0.70-2.52
	Stereotyped utterances	0.85	0.49-1.46
	Inappropriate questions	1.03	0.59-1.80
	Pronoun reversal	1.53	0.89-2.64
	Neologisms	1.10	0.64-1.90
	Social chat	0.99	0.52-1.90
	Social chat (verbal only)	0.71	0.42-1.22
	Imitation	**0.34***	**0.19-0.59**
	Pointing to express interest	0.99	0.58-1.71
	Gestures	0.87	0.51-1.49
	Nodding to mean 'yes'	1.06	0.61-1.83
	Head shaking to mean 'no'	0.95	0.55-1.64
	Imitative social play	**0.24***	**0.13-0.42**
	Imaginative social play	0.80	0.43-1.52
Reciprocal Social Interaction	**Inappropriate facial expressions**	**0.51***	**0.27-0.95**
	Use of other's body to communicate	1.04	0.58-1.87
	Friends	0.82	0.47-1.43
	Eye gaze	**0.48***	**0.28-0.84**
	Social smiling	**0.57***	**0.33-0.99**
	Showing and directing attention	1.15	0.67-1.97
	Offering to share	0.64	0.35-1.18
	Seeking to share enjoyment	0.63	0.37-1.10
	Offering comfort	**0.45***	**0.26-0.78**
	Quality of social overtures	**0.49***	**0.27-0.88**
	Range of facial expressions	**0.50***	**0.29-0.86**
	Interest in children	0.61	0.32-1.16
	Response to other children's approaches	**0.46***	**0.26-0.83**
	Imaginative play with peers	1.65	0.56-4.83
	Group play	0.70	0.34-1.44
Restricted, Repetitive & Stereotyped Behaviour	Verbal rituals	1.03	0.60-1.77
	Compulsions and rituals	**3.29***	**1.66-6.52**
	Unusual preoccupations	0.90	0.52-1.58
	Repetitive use of objects	0.94	0.52-1.70

Circumscribed interests	0.91	0.52-1.56
Unusual sensory interests	0.59	0.34-1.02
Hand and finger mannerisms	0.89	0.50-1.61
Complex body mannerisms	0.73	0.42-1.25

*****Significant (value of 1.00 lies outside the 99% confidence interval)

[a]Items in bold differ significantly between groups

Table 3. SDQ scores in DS+ASD and ASD groups

SDQ	Group	Median (IQR)	Group difference*
Total	DS+ASD	17.0 (13-21)	z=2.40
	ASD	19.0 (15-22)	p < .001; d = .15
Subscale*			
Emotional symptoms	DS+ASD	3.0 (1-4)	z=3.82
	ASD	4.0 (2.5)	p < .001; d = .23
Conduct problems	DS+ASD	3.0 (2-4)	z=-.62
	ASD	3.0 (2-4)	p = .54; d = .04
Hyperactivity	DS+ASD	7.0 (5-9)	z=-.55
	ASD	7.0 (5-9)	p = .59; d = .03
Peer problems	DS+ASD	5.0 (3-6)	z=3.35
	ASD	5.0 (4-7)	p < .005; d = .20
Prosocial behaviour	DS+ASD	5.0 (3-7)	z=-1.71
	ASD	4.0 (2-6)	p = .09; d = .10

*Mann Whitney z; Cliff's d